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Research article

Effect of selective sleep deprivation on heart rate variability in post-90s healthy volunteers

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Abstract: The 5-minute frequency domain method was used to examine the effects of polysomnography (PSG)-guided acute selective sleep deprivation (REM/SWS) on the cardiovascular autonomic nervous system, heart rate, and rhythm in healthy volunteers to understand the relationship between cardiac neuro regulatory homeostasis and cardiovascular system diseases in healthy subjects. The study included 30 healthy volunteers selected through the randomized-controlled method, randomly divided into REM sleep deprivation and SWS sleep deprivation groups. PSG analyses and dynamic electrocardiogram monitoring were done at night, during slow wave sleep or REM sleep. An all-night sleep paradigm, without any interruptions, was tested 3 times for comparison. The frequency domain parameter method was further used to monitor the volunteers 5 min before and after a period of sleep deprivation. According to the characteristics of the all-night sleep scatter plot, healthy volunteers were divided into abnormal and normal scatter plot groups. When compared with the period before sleep deprivation, high frequency (HF) and normalized high-frequency component (HFnu) were found to be decreased. Normalized low-frequency component (LFnu) increased in the abnormal scatter plot group after sleep deprivation, and this difference was statistically significant ($P < 0.05$). The scatter plot also showed that very low frequency (VLF) increased only in the normal group after deprivation and this difference, as well, was statistically significant ($P < 0.05$). The increase in diastolic blood pressure in the abnormal group was statistically significant ($P < 0.05$), but the change in blood pressure in the normal group was not statistically significant ($P > 0.05$). There are 62.5% of the patients and 20% of the employees that

were observed to have abnormal whole-night sleep patterns during the uninterrupted whole-night sleep regime. Patients with atrial or ventricular premature beats (more than 0.1%), and those with ST-t changes during sleep, were all ascertained as abnormal. We concluded that some healthy people could face unstable autonomic nervous functioning related to their long-term tension, anxiety, time urgency, hostility, and other chronic stress states. In the face of acute sleep deprivation selectivity, mild stress based excitability of the vagus nerve is reduced, which diminishes the protective function, making them susceptible to conditions such as premature ventricular arrhythmia.

Keywords: healthy volunteers; PSG; selective sleep deprivation; autonomic nervous system; heart rate variability

1. Introduction

Sleep is a natural process of mental and physical state restoration, characterized by various mechanisms which entail changes in consciousness, relatively inhibited sensory activity, reduced activity of muscles (almost all voluntary muscles are inhibited during rapid eye movement), and a reduced interaction with the surrounding environment. The difference between sleep and wakefulness is that the ability to respond to stimuli is reduced in the state of sleep, though being more reactive than during a coma or any disturbances in the consciousness. Sleep represents a different yet unique, active brain pattern [1] and plays a vital role in the physical and mental health of humans [2,3]. Adequate high-quality sleep is essential to maintain normal body metabolism and reduce the incidence of certain diseases and the following morbidity or mortality.

Sleep deprivation, refers to an insufficient period of sleep and/or sleep quality required to maintain an individual's optimum alertness, performance, and health. Such symptoms are either chronic or acute, with various patterns of severity. Acute insufficient sleep refers to a condition where individuals sleep less than usual, or not at all, for a short period of time (usually lasting one to two days). Chronic (long-term) insufficient sleep refers to a condition in individuals sleeping for significantly less amount of time vis-à-vis the ideal duration. Prolonged insufficient sleep is frequently used interchangeably with insomnia even though they are quite different. Although long-term insufficient sleep and insomnia both represent reduced sleep duration and/or quality along with impaired physical functions, the distinction between them lies in the basic ability to fall asleep. Sleep deprived individuals could quickly fall asleep under normal circumstances, but those with insomnia find it insanely hard to just fall asleep [4,5].

Sleep deprivation is known to increase the risk of cardiovascular disease, obesity, and diabetes. Clinical trials have shown that Sleep deprivation alters the stability of the cardiovascular autonomic nervous system and thereby attenuate autonomic responses [6]. Cardiac sinus rhythm and heart rate variability (HRV) are mainly regulated by sympathetic and parasympathetic nerves, where HRV is the best non-invasive parameter that can be monitored for cardiac autonomic regulation analysis [7], and the 5-minute frequency domain method is widely used to assess cardiovascular, neurological regulation during sleep [8]. In this study, healthy volunteers were selected for selective sleep deprivation, notably for the first time in China. The HRV in post-90s was analyzed by the 5-minute frequency domain method.

2. Data and methods

2.1. Study subjects; inclusion and exclusion criteria

The study was approved by the medical ethics committee of Qingdao Central Hospital, with the approval number-KY-P201807501, and the clinical trial was registered online under the registration number-ChiCTR190020622. All healthy volunteers were recruited and fully briefed regarding the aim of the study and evaluation methods before the test, and they subsequently signed the informed consent form. Clinical screening included detailed medical history inquiry, physical examination, basic cardiac examination (cardiac function, blood pressure, ECG, etc.), and an evaluation questionnaire. The inclusion criteria were as follows: Aged between 20–39 years; have stable, regular sleep and daily work activities one week before the test; no irregular work shifts during last three months. The exclusion criteria were as follows: Body mass index of more than 30 kg/m^2; acute or (and) chronic cardiopulmonary diseases; smoking more than 10 cigarettes/day; chronic alcoholism; current facing adverse life events; abnormal results in the physical and neurological examination; pregnant or lactating women; any form of sleep apnea, etc. The research procedure of the experiment was carried out in accordance with the Declaration of Helsinki (2000). The volunteers were compensated financially after the completion of the experiments.

2.2. Trial procedure

Thirty volunteers (male:female = 1:1, age 26.27 ± 4.479 years) eventually fulfilled the inclusion and exclusion criteria, and they were randomly divided into two groups, the rapid eye movement (REM) sleep deprivation group and slow wave (SWS) sleep deprivation group. All subjects were encouraged to maintain a regular sleep time, from 10:00 pm to 7:00 am, from one week before the trial. The experiments were conducted for three consecutive days: normal sleep on the first day (excluding the first night effect and screening for exclusion criteria during sleep), selective sleep deprivation on the second day, followed by normal sleep on the third day. PSG and ambulatory electrocardiograms were monitored at night, from 21:00 on that day to 07:00 on the next day. Sleep deprivation causes awakening while entering SWS or REM sleep in the evening. Methods for waking up included turning on the light and playing a cell phone ring tone of certain decibels. For subjects who missed the alarm and woke up after 3 min, the physical intervention was used to keep them awake for 5 min, after which lights were turned off to begin the next cycle of sleep. The subjects were allowed to sleep regularly until 7:00 am, after the deprivation, and allowed to work while they were studied throughout the day. Blood pressures, systolic and diastolic, were monitored before going to bed and after waking up.

2.3. Data acquisition

Sleep stage was determined by the synchronous acquisition of data via PSG signals; Holter monitoring was performed and data recorded using a Holter recorder (ct-086, ct-082 and ct-083s) manufactured by Hangzhou Baihui Medical Equipment Co. Ltd., and the data were analyzed using the latest software (v1.0.0). Frequency domain analysis of HRV was performed on consecutive 5-min Holter data, without interference, before and after the selective sleep deprivation. The

frequency-domain analysis metrics were as follows: LF: low frequency, HF: High frequency, LF/HF: low frequency/high frequency ratio. LF represents sympathetic tension or a cardiac sympathetic tension with vagal co-innervation. HF is a marker of cardiac vagal tone. The LF/HF ratio is a more sensitive indicator reflecting the sympatho-vagal balance [9]. The significance of VLF is still debated, but it has been suggested that it may reflect the function of the renin-angiotensin system and/or thermoregulatory processes [10].

2.4. Statistical analysis

The SPSS24.0 software was used for statistical processing. Normally distributed measures were expressed as $X \pm S$, and paired t-tests were used for before-and-after comparison. $P < 0.05$ was taken as the statistically significant difference.

3. Results

3.1. Baseline conditions of participating study patients

Fifty healthy volunteers were screened and 30 were ultimately recruited for the study, out of which 20 were fifth-year clinical internship students and 10 were employees. One among the slow-wave sleep deprivation group was excluded from the trial due to a slow-wave sleep deficit on the night of sleep deprivation, and three people were not included due to incomplete recording of trial data. Twenty-six people were finally included in the statistical analysis.

3.2. Scatter plot of the whole night sleep

Healthy volunteers were divided into two groups according to the characteristics of the scatter plot for the whole night sleep: the abnormal scatter plot group and the normal scatter plot group. Scattergram for the abnormal group (12 people, 10 medics, male:female = 1:1, REM:SWS = 1:1) and the normal group (14 people, 6 medic, male:female = 1:1, REM:SWS=1:1) had baseline characteristics as in Table 1.Scattergrams for the whole sleep time domain are as in Figures 1 and 2.

Table 1. Healthy volunteer baseline characteristics ($X \pm S$).

Items	Scatter plot anomaly group	Scatter plot normal group
Age, year	24.33 ± 3.52	27.86 ± 4.33
Height, cm	169.33 ± 8.60	168.93 ± 8.11
Weight, Kg	66.00 ± 13.31	69.46 ± 20.55
BMI, kg/m^2	23.31 ± 3.49	22.62 ± 3.19
Heart rate, bpm	68.75 ± 7.52	74.93 ± 8.39
Systolic pressure, mmHg	113.50 ± 14.64	114.86 ± 12.31
Diastolic pressure, mmHg	67.83 ± 8.00	72.29 ± 10.64

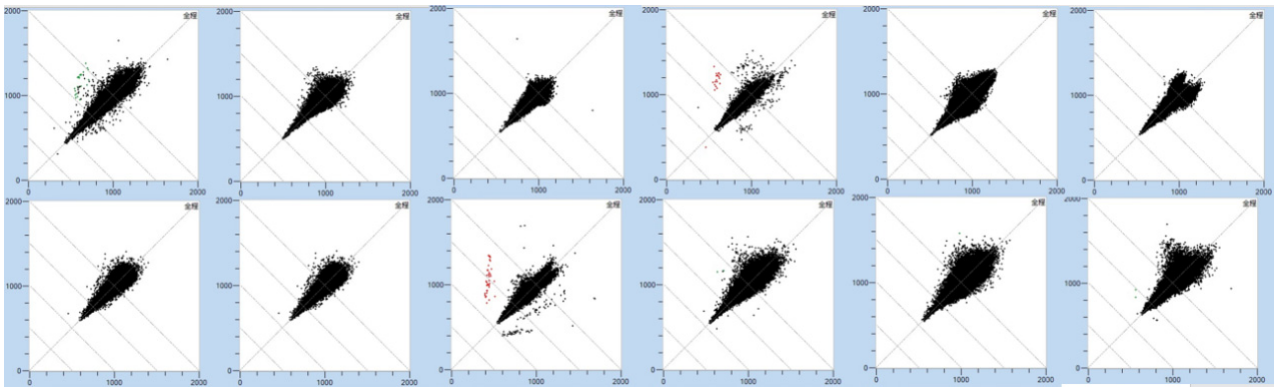

Figure 1. Abnormal scatter plots in healthy volunteers.

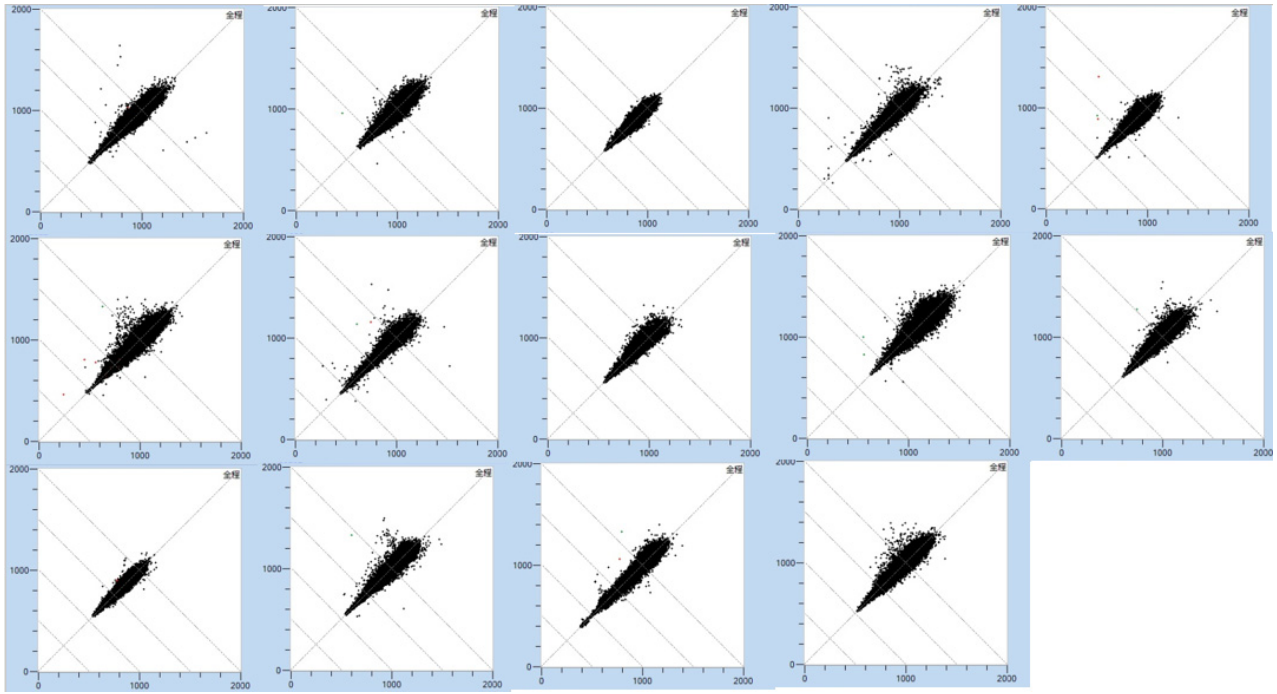

Figure 2. Normal scatter plots in healthy volunteers.

3.3. Scatter plot after sleep deprivation

HF and HFnu decreased whereas LFnu increased in the scatter plot abnormal group after sleep deprivation when compared with the period before deprivation, and the differences were statistically significant ($P < 0.05$). Only VLF increased in the scatter plot normal group after deprivation, and the differences were again statistically significant ($P < 0.05$), as shown in Table 2.

3.4. Blood pressure

The scattergram for the abnormal group showed elevated diastolic blood pressure after waking

up post sleep deprivation and the difference was statistically significant ($P < 0.05$), while the scattergram for the normal group did not show a statistically significant difference in blood pressure ($P > 0.05$) (Table 3).

3.5. Other indicators

Sixteen medics were included in the analysis, out of which 10 (62.5%) had abnormal scattergrams throughout the night, while only 2 employees (20%) had abnormal scatter grams under the same scenario. Volunteers with atrial/ventricular premature beats (greater than 0.1%) and ST-T changes during sleep were considered abnormal in the scatter gram results (see Table 4).

Table 2. Data of 5-min frequency domain HRV analysis before and after sleep deprivation (X ± S).

Frequency domain analysis index	Scatter plot anomaly group			Scatter plot normal group		
	5 min before Sleep deprivation	5 min after Sleep deprivation	P value	5 min before Sleep deprivation	5 min after Sleep deprivation	P value
VLF	2577 ± 3058	3033 ± 2222	0.498	1496 ± 1506	2906 ± 2396	0.043
LF	832 ± 565	1025 ± 884	0.309	678 ± 450	1040 ± 616	0.132
HF	1351 ± 764	902 ± 725	0.020	771 ±402	611 ± 342	0.215
LF/HF	0.84 ± 0.91	1.35 ± 0.89	0.191	1.12 ±0.86	2.37 ± 2.34	0.063
LFnu	38.88 ± 16.41	52.57 ± 15.34	0.026	46.32 ±18.40	59.94 ± 19.17	0.115
HFnu	61.12 ± 16.42	47.43 ± 15.34	0.026	53.68 ±18.40	40.06 ± 19.17	0.115

Table 3. Changes in blood pressure before and after sleep deprivation (X ± S).

Items	Natural sleep		sleep deprivation		Sleep recovery	
	systolic pressure (mmHg)	diastolic pressure (mmHg)	systolic pressure (mmHg)	diastolic pressure (mmHg)	systolic pressure (mmHg)	diastolic pressure (mmHg)
Scatter plot anomaly group						
Beforebed	111 ± 9.89	69 ± 5.59	107 ± 10.58	64 ± 4.27	109 ± 13.32	63 ± 10.64
Afterawake	115 ± 10.52	70 ± 8.64	111 ± 12.06	67 ± 6.25	110 ± 10.60	67 ± 5.46
P value	0.093	0.605	0.083	0.038	0.742	0.178
Scatter plot normal group						
Beforebed	109 ± 13.15	65 ± 4.97	103 ± 3.09	61 ± 4.52	106 ± 11.75	63 ± 6.39
Afterawake	110 ± 10.07	68 ± 7.71	107 ± 11.67	65 ± 7.82	108 ± 8.27	67 ± 6.80
P value	0.670	0.212	0.216	0.007	0.504	0.146

Table 4. Subgroup personnel characteristics statistics.

Items	Abnormal group (n = 12)		Normal group (n = 14)	
	Number	proportion	Number	proportion
ST-T alterations	3	25%	0	0
Premature atrial/ventricular (≥ 0.1%)	3	25%	0	0

4. Discussion

The functional activity of the cardiac autonomic nervous system is regulated at dynamic equilibrium at all times due to changes in the environment and physiological state, and hence normal individuals are able to tolerate slight fluctuations, whereas those with respiratory or cardiovascular diseases are prone to long-term imbalance. The human heart is innervated by both sympathetic and vagal nerves, and cardiac activity, at rest, is controlled by continuous tonic inhibition of the parasympathetic nervous system [11]. In contrast, sympathetic excitation predominates in a state of fatigue, excitement, and stress conditions in people. Reduced HRV is considered as a marker of heart disease. Parasympathetic regulation is vital in the pathophysiology of cardiovascular disease and other related complications and is also associated with reduced dynamic flexibility, reduced complexity, and increased overall vulnerability [12].

In this study, we found that those with abnormal scattergrams showed significantly lower vagal activity (reduced HF, HFnu) and elevated sympathetic (LFnu) innervations after sleep deprivation, whereas those with normal scattergrams showed elevated VLF only after the deprivation. The results suggest that sleep deprivation is more likely to imbalance sympatho-vagal regulation in a population with sub-stable autonomic regulation, as elucidated by significantly reduced parasympathetic activity and relatively hyperactive sympathetic output. In contrast, in subjects with normal scatter grams, there was no significant change in HRV before and after selective deprivation, and the autonomic nervous system regulation was more able to adapt to sudden changes in the environment. It has been reported that after 24 h of sleep deprivation, both HR and BP were higher than the baseline level in healthy volunteers [12], and one of the possible mechanisms could be related to enhanced sympathetic activity. Significant alterations in autonomic function after chronic sleep deprivation [13], characterized by an overactive sympathetic drive and corresponding underactive parasympathetic drive, are risk factors for cardiovascular disease and mortality [14]. For those with unstable scatter grams in the face of sleep deprivation, auto regulation is reduced, which weakens vagal function. The shift from sympathetic vagal balance to sympathetic dominance and parasympathetic withdrawal causes alterations in heart rate, blood pressure, and premature atrio-ventricular contractions, while chronic stress can lead to chronic stress cardiovascular disease.

The results of blood pressure analysis after selective sleep deprivation, after three bouts of sleep deprivation in the abnormal scattergram group, showed that the diastolic blood pressure was higher after waking up than before sleep, while the change in systolic blood pressure was not statistically significant. There was no significant change in blood pressure after waking up in the normal scattergram group. Some studies have reported diastolic hypertension alone as a specific pattern of hypertension associated with sleep breathing disorders, especially in the early stages of the disease [15]. Diastolic blood pressure may be a potential marker for early identification of cardiovascular consequences in OSA patients. An elevated diastolic blood pressure is usually considered to be

associated with an increase in peripheral resistance, which is mainly determined by small arteries, while systolic blood pressure is predominantly influenced by medium to large vessels [16]. In the absence of an elevated systolic blood pressure, an elevated diastolic blood pressure would suggest that repeated sleep deprivation would have a more pronounced effect on the peripheral vasculature than on the medium to large vessels. Sleep deprivation-induced increases in peripheral resistance and fluctuations in blood pressure are attributed to sympathetic activation [17], but changes in sympathetic activity do not always coincide with changes in blood pressure. The exact mechanisms for this observation need to be further explored.

The results of this study showed that autonomic instability was significantly higher in medical interns (62.5%) than in corporate employees (20%), and the number of atrial premature beats or ventricular premature beats (greater than 0.1%) and ST-T changes during sleep were found to be higher in those with autonomic instability, suggesting that those with autonomic dysfunction are more likely to have atria/ventricular premature beats along with other heart rate arrhythmias and ST-T changes. As a specialized group of people, medics are under the double pressure of exam preparation and clinical practice and are accompanied by poor lifestyle and dietary habits, resulting in psychological stress, emotional agitation, abnormal behavior, and hostility, which lead to the excitation of the limbic system, over-activation of the sympathetic nervous system and under-activation of the parasympathetic nervous system, and are more vulnerable to autonomic dysfunction. In stressful situations, both the central and peripheral nervous system undergo corresponding changes since the sympathetic activity of the innervated heart increases and the vagal activity decreases, resulting in increased heart rate, decreased HRV, and increased cardiac metabolic demand, all of which can cause myocardial ischemia, arrhythmia and sudden death in severe cases [18].

5. Conclusions

Instability of autonomic function is found in some healthy individuals, which may be related to their chronic stress, such as tension, anxiety, time urgency, and hostility. In the face of mild stress conditions such as acute selective sleep deprivation, these individuals can exhibit sympathetic and parasympathetic imbalance, and reduced excitability of the vagus nerve, which make them more prone to premature arrhythmias and instability of blood pressure regulation, ST-T changes, etc. Therefore, the administration of targeted measures, such as advanced screening, coping measures, and imparting health education (exercise, sleep, and music prescriptions, for example) to populations sub-healthyin terms of autonomic function, can reduce the occurrence of cardiovascular disease and sudden death, which is especially significant for certain examples of special operating populations.

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